

REMARKS

Status of the Claims

Pending claims

Claims 1-16 as filed are pending.

The Restriction Requirement

The Patent Office has alleged that the pending claims of the application are directed to two separate and distinct inventions under 35 U.S.C. §121:

The Election

In response to the Restriction Requirement, Applicants elect Group I, claims 1-16 wherein X is C.

Applicant believes that no fee is required for submission of this Response. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 06-1050. Please credit any overpayment to the above-noted Deposit Account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858 678 5070.

Respectfully submitted,

Date: 12/4/02


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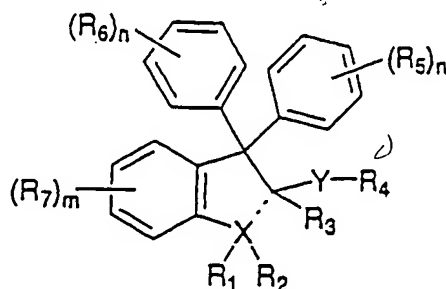
Version with markings to show changes made

In the claims:

Claims 1, 3, 4, 6, 7, and 11 have been amended as follows:

1. A compound having the structural formula:

(I)



or a pharmaceutically acceptable salt or hydrate thereof,
wherein:

m is 0, 1, 2, 3 or 4;

each n is independently 0, 1, 2, 3, 4 or 5;

X is C [or N];

Y is absent, (C₁-C₆) alkyl, (C₁-C₆) alkenyl or (C₁-C₆)
alkynyl;

R₁ is absent, -OR, -SR, =O, =S, =N-OR, -O-C(O)R, -S-C(O)R,
-O-C(S)R, -S-C(S)R, or when taken together with R₂ is a 3-8
membered heterocycloalkyl or a substituted 3-8 membered
heterocycloalkyl;

R₂ is absent or -H;

R₃ is absent or -H;

R₄ is -H, -OR', -SR', -NR'₂, -CN, -NO₂, (C₃-C₈) cycloalkyl,
3-8 membered heterocycloalkyl, -C(O)R', -C(S)R', -C(O)OR',
-C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'₂ or -C(S)NR'₂;

each R₅, R₆ and R₇ is independently selected from the
group consisting of -halogen, -R', -OR', -SR', -NR'₂, -ONR'₂,
-SNR'₂, -NO₂, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(O)SR',
-C(S)OR', -CS(S)R', -C(O)NR'₂, -C(S)NR'₂, -C(O)NR'(OR'),
-C(S)NR'(OR'); -C(O)NR'(SR'), -C(S)NR'(SR'), -CH(CN)₂,
-CH[C(O)R']₂, -CH[C(S)R']₂, -CH[C(O)OR']₂, -CH[C(S)OR']₂,
-CH[C(O)SR']₂ and -CH[C(S)SR']₂;

each R is independently selected from the group consisting of -H, (C₁-C₆) alkyl, (C₁-C₆) alkenyl, (C₁-C₆) alkynyl, (C₅-C₂₀) aryl, substituted (C₅-C₂₀) aryl, (C₆-C₂₆) alkaryl and substituted (C₆-C₂₆) alkaryl;

the heterocycloalkyl substituents are each independently selected from the group consisting of -CN, -NO₂, -NR'₂, -OR', -C(O)NR'₂, -C(S)NR'₂, -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR' and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of halogen, -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'₂, -C(S)NR'₂ and trihalomethyl;

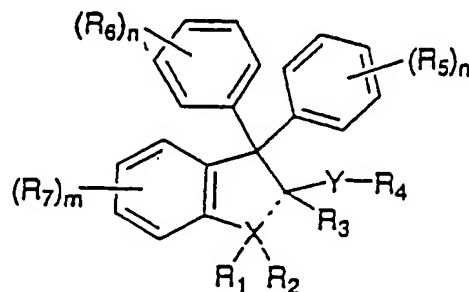
each R' is independently selected from the group consisting of -H, (C₁-C₆) alkyl, (C₁-C₆) alkenyl and (C₁-C₆) alkynyl;

--- designates a single or double bond; and

wherein when X is C and R₁ is =O or -OH, at least one of R₅, R₆ or R₇ is other than -H, or Y is present or R₄ is other than -H and when X is N, --- is a double bond and R₁, R₂, R₃ and Y are absent, R₄ is other than -NH₂.

3. A pharmaceutical composition comprising a compound and a pharmaceutically acceptable excipient, carrier or diluent, said compound having the structural formula:

(I)



or a pharmaceutically acceptable salt or hydrates thereof,
wherein:

m is 0, 1, 2, 3 or 4;

each n is independently 0, 1, 2, 3, 4 or 5;

X is C [or N];

Y is absent, (C₁-C₆) alkyl, (C₁-C₆) alkenyl or (C₁-C₆)
alkynyl;

R₁ is absent, -OR, -SR, =O, =S, =N-OR, -O-C(O)R, -S-C(O)R,
-O-C(S)R, -S-C(S)R, or when taken together with R₂ is a 3-8
membered heterocycloalkyl or a substituted 3-8 membered
heterocycloalkyl;

R₂ is absent or -H;

R₃ is absent or -H;

R₄ is -H, -OR', -SR', -NR'₂, -CN, -NO₂, (C₁-C₈) cycloalkyl,
3-8 membered heterocycloalkyl, -C(O)R', -C(S)R', -C(O)OR',
-C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'₂ or -C(S)NR'₂;

each R₅, R₆ and R₇ is independently selected from the
group consisting of -halogen, -R', -OR', -SR', -NR'₂, -ONR'₂,
-SNR'₂, -NO₂, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(O)SR',
-C(S)OR', -C(S)SR', -C(O)NR'₂, -C(S)NR'₂, -C(O)NR'(OR'),
-C(S)NR'(OR'); -C(O)NR'(SR'), -C(S)NR'(SR'), -CH(CN)₂,
-CH[C(O)R']₂, -CH[C(S)R']₂, -CH[C(O)OR']₂, -CH[C(S)OR']₂,
-CH[C(O)SR']₂ and -CH[C(S)SR']₂;

each R is independently selected from the group
consisting of -H, (C₁-C₆) alkyl, (C₁-C₆) alkenyl, (C₁-C₆)
alkynyl, (C₅-C₂₀) aryl, substituted (C₅-C₂₀) aryl, (C₆-C₂₆)
alkaryl and substituted (C₆-C₂₆) alkaryl;

the heterocycloalkyl substituents are each independently
selected from the group consisting of -CN, -NO₂, -NR'₂, -OR',
-C(O)NR'₂, -C(S)NR'₂, -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR'
and trihalomethyl;

the aryl and alkaryl substituents are each independently
selected from the group consisting of halogen, -C(O)R',
-C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', -C(O)NR'₂,
-C(S)NR'₂ and trihalomethyl;

each R' is independently selected from the group consisting of -H, (C₁-C₆) alkyl, (C₁-C₆) alkenyl and (C₁-C₆) alkynyl; and

--- designates a single or double bond.

4. The pharmaceutical composition of Claim 3, wherein in the compound of structural formula (I):

m is 0 or 1;

each n is independently 0 or 1;

X is C [or N];

Y is absent, (C₁-C₃) alkyl, (C₁-C₃) alkenyl or (C₁-C₃) alkynyl;

R₁ is absent -H, -OR, =O, -NR₂, =N-OR, -O-C(O)R, or when taken together with R₂ is 3-5 membered oxirane or 3-5 membered substituted oxirane;

R₂ is absent or -H;

R₃ is absent or -H;

R₄ is -H, -OR, -NR₂, -CN, -C(O)OR, -C(O)NR₂ or 5-6 membered dioxycycloalkyl;

each R₅, R₆ and R₇ is independently selected from the group consisting of -R', -F, -Cl or -Br;

each R is independently selected from the group consisting of -H, (C₁-C₃) alkyl, (C₁-C₃) alkenyl, (C₁-C₃) alkynyl, (C₅-C₁₀) aryl, substituted (C₅-C₁₀) aryl, (C₆-C₁₁) alkaryl, substituted C₆-C₁₁ alkaryl;

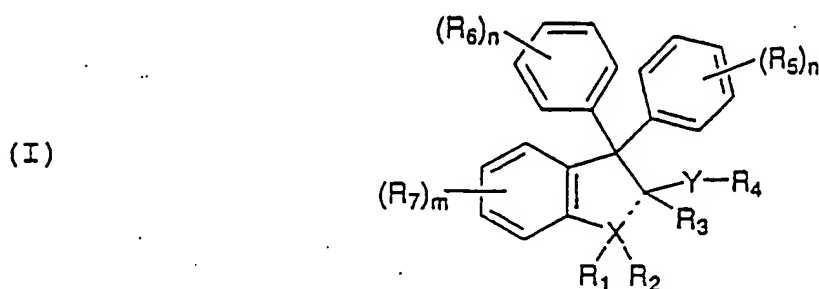
the oxirane substituent is -CN, -NO₂, -NR'₂, -OR' and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of -F, -Cl, -Br, -CN, -NO₂, -NR'₂, -C(O)R', -C(O)OR' and trihalomethyl;

R' is -H, (C₁-C₃) alkyl, (C₁-C₃) alkenyl or (C₁-C₃) alkynyl; and

--- is a single or double bond.

6. A method of inhibiting mammalian cell proliferation, said method comprising the step of contacting a mammalian cell *in situ* with an effective amount of a compound having the structural formula:



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

m is 0, 1, 2, 3 or 4;

each n is independently 0, 1, 2, 3, 4 or 5;

X is C [or N];

Y is absent, (C_1-C_6) alkyl, (C_1-C_6) alkenyl or (C_1-C_6) alkynyl;

R_1 is absent, $-OR$, $-SR$, $=O$, $=S$, $=N-OR$, $-O-C(O)R$, $-S-C(O)R$, $-O-C(S)R$, $-S-C(S)R$, or when taken together with R_2 is a 3-8 membered heterocycloalkyl or a substituted 3-8 membered heterocycloalkyl;

R_2 is absent or $-H$;

R_3 is absent or $-H$;

R_4 is $-H$, $-OR'$, $-SR'$, $-NR'_2$, $-CN$, $-NO_2$, (C_1-C_8) cycloalkyl, 3-8 membered heterocycloalkyl, $-C(O)R'$, $-C(S)R'$, $-C(O)OR'$, $-C(S)OR'$, $-C(O)SR'$, $-C(S)SR'$, $-C(O)NR'_2$ or $-C(S)NR'_2$;

each R_5 , R_6 and R_7 is independently selected from the group consisting of $-halogen$, $-R'$, $-OR'$, $-SR'$, $-NR'_2$, $-ONR'_2$, $-SNR'_2$, $-NO_2$, $-CN$, $-C(O)R'$, $-C(S)R'$, $-C(O)OR'$, $-C(O)SR'$, $-C(S)OR'$, $-CS(S)R'$, $-C(O)NR'_2$, $-C(S)NR'_2$, $-C(O)NR'(OR')$,

$-\text{C}(\text{S})\text{NR}'(\text{OR}')$; $-\text{C}(\text{C})\text{NR}'(\text{SR}')$, $-\text{C}(\text{S})\text{NR}'(\text{SR}')$, $-\text{CH}(\text{CN})_2$,
 $-\text{CH}[\text{C}(\text{O})\text{R}']_2$, $-\text{CH}[\text{C}(\text{S})\text{R}']_2$, $-\text{CH}[\text{C}(\text{O})\text{OR}']_2$, $-\text{CH}[\text{C}(\text{S})\text{OR}']_2$,
 $-\text{CH}[\text{C}(\text{O})\text{SR}']_2$ and $-\text{CH}[\text{C}(\text{S})\text{SR}']_2$;

each R is independently selected from the group consisting of -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, $(\text{C}_5-\text{C}_{20})$ aryl, substituted $(\text{C}_5-\text{C}_{20})$ aryl, $(\text{C}_6-\text{C}_{25})$ alkaryl and substituted $(\text{C}_6-\text{C}_{26})$ alkaryl;

the heterocycloalkyl substituents are each independently selected from the group consisting of -CN, $-\text{NO}_2$, $-\text{NR}'_2$, $-\text{OR}'$, $-\text{C}(\text{O})\text{NR}'_2$, $-\text{C}(\text{S})\text{NR}'_2$, $-\text{C}(\text{O})\text{OR}'$, $-\text{C}(\text{S})\text{OR}'$, $-\text{C}(\text{O})\text{SR}'$, $-\text{C}(\text{S})\text{SR}'$ and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of halogen, $-\text{C}(\text{O})\text{R}'$, $-\text{C}(\text{S})\text{R}'$, $-\text{C}(\text{O})\text{OR}'$, $-\text{C}(\text{S})\text{OR}'$, $-\text{C}(\text{O})\text{SR}'$, $-\text{C}(\text{S})\text{SR}'$, $-\text{C}(\text{O})\text{NR}'_2$, $-\text{C}(\text{S})\text{NR}'_2$ and trihalomethyl;

each R' is independently selected from the group consisting of -H, (C_1-C_6) alkyl, (C_1-C_6) alkenyl and (C_1-C_6) alkynyl; and

--- designates a single or double bond.

7. The method of Claim 6, wherein in the compound of structural formula (I):

m is 0 or 1;

each n is independently 0 or 1;

X is C [or N];

Y is absent, (C_1-C_3) alkyl, (C_1-C_3) alkenyl or (C_1-C_3) alkynyl;

R_1 is absent -H, -OR, =O, $-\text{NR}_2$, =N-OR, -O-C(O)R, or when taken together with R_2 is 3-5 membered oxirane or 3-5 membered substituted oxirane;

R_2 is absent or -H;

R_3 is absent or -H;

R_4 is -H, -OR, $-\text{NR}_2$, -CN, -C(O)OR, -C(O)NR₂ or 5-6 membered dioxycycloalkyl;

each R_5 , R_6 and R_7 is independently selected from the group consisting of -R', -F, -Cl or -Br;

each R is independently selected from the group consisting of -H, (C₁-C₃) alkyl, (C₁-C₃) alkenyl, (C₁-C₃) alkynyl, (C₅-C₁₀) aryl, substituted (C₅-C₁₀) aryl, (C₆-C₁₃) alkaryl, substituted C₆-C₁₃) alkaryl;

the oxirane substituent is -CN, -NO₂, -NR'₂, -OR' and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of -F, -Cl, -Br, -CN, -NO₂, -NR'₂, -C(O)R', -C(O)OR' and trihalomethyl;

R' is -H, (C₁-C₃) alkyl, (C₁-C₃) alkenyl or (C₁-C₃) alkynyl; and

--- is a single or double bond.

11. The method of Claim 10, wherein in the compound of structural formula (I):

m is 0 or 1;

each n is independently 0 or 1;

X is C [or N];

Y is absent, (C₁-C₃) alkyl, (C₁-C₃) alkenyl or (C₁-C₃) alkynyl;

R₁ is absent -H, -OR, =O, -NR₂, =N-OR, -O-C(O)R, or when taken together with R₂ is 3-5 membered oxirane or 3-5 membered substituted oxirane;

R_1 is absent or -H;

R_2 is absent or -H;

R_3 is -H, -OR, -NR₂, -CN, -C(O)OR, -C(O)NR₂ or 5-6 membered dioxycycloalkyl;

each R_4 , R_5 and R_6 is independently selected from the group consisting of -R', -F, -Cl or -Br;

each R is independently selected from the group consisting of -H, (C₁-C₃) alkyl, (C₁-C₃) alkenyl, (C₁-C₃) alkynyl, (C₅-C₁₀) aryl, substituted (C₅-C₁₀) aryl, (C₆-C₁₃) alkaryl, substituted C₆-C₁₃) alkaryl;

the oxirane substituent is -CN, -NO₂, -NR'₂, -OR' and trihalomethyl;

the aryl and alkaryl substituents are each independently selected from the group consisting of -F, -Cl, -Br, -CN, -NO₂, -NR'₂, -C(O)R', -C(O)OR' and trihalomethyl;

R' is -H, (C₁-C₃) alkyl, (C₁-C₃) alkenyl or (C₁-C₃) alkynyl; and

--- is a single or double bond.